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(54) Title: GLYCOSAMINOGLYCAN DERIVATIVES AND THEIR USE AS INHIBITORS OF TUMOR INVASIVENESS OR METASTATIC PROFUSION-II

(57) Abstract

The present invention comprises a method for impeding the formation of tumor metastasis or tumor invasiveness in a host. Such inhibition comprises administration to the host of a glycosaminoglycan derivative substantially devoid of anticoagulation activity and is an effective inhibitory of heparanase activity. Such a glycosaminoglycan derivative may be provided by purchase or synthesis as directed herein. Parenteral administration to a tumor-bearing host of the glycosaminoglycan derivative results in the exposure of host-borne tumor cells thereto. Such exposure to effective levels of the derivative results in the inhibition of tumor heparanase activity and a lessening of invasiveness and metastatic spread. Heparin, a glycosaminoglycan particularly effective as a heparanase inhibitor and an anti-clotting agent, is a preferred glycosaminoglycan for derivatization. Upon derivatization according to the present invention heparin may be converted into a glycosaminoglycan derivative substantially devoid of anticoagulant activity but yet being an effective inhibitor of heparanase activity. Mere reduction of heparin carboxyl groups results in the production of a glycosaminoglycan derivative inhibitory to heparanase activity but without substantially anticoagulant activity non-anticoagulating, heparanase-inhibiting glycosaminoglycan derivatives may also be prepared from heparin, for example, by: at least partial N-desulfation and then N-acetylation; or N-, O-desulfation followed by N-resulfation.

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